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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,188	07/10/2001	Henrik Bisgard-Frantzen	4318.224-US	7527

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EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	15

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/902,188	Applicant(s) Bisgaard-Frantzen et al.
	Examiner Rebecca Prouty	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 25, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *68-139* is/are pending in the application.

4a) Of the above, claim(s) *78-85, 96-103, 114-121, and 132-139* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *68-77, 86-95, 104-113, and 122-131* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11,12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-67 have been canceled. Claims 68-139 are at issue and are present for examination.

Applicant's election without traverse of Group I, Claims 68-77, 86-95, 104-113, and 122-131 in Paper No. 14 is acknowledged.

Claims 78-85, 96-103, 114-121, and 132-139 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 14.

Claims 74, 92, 110, and 128 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are confusing and improperly dependent as they recite limitations which are excluded from the genus of alpha amylases of the claims from which they depend. It is suggested that they be amended to recite "An isolated alpha amylase comprising an alpha amylase of claim 73 (or 91, 109, or 126) having amino acid substitutions of cysteine at positions equivalent to 349 and 428 of SEQ ID NO:3."

Claims 68-72, 86-90, 104-108, and 122-126 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of variant α-amylases having at least two mutations (i.e., deletion of residues equivalent to 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3). The specification teaches the structure of only a few representative species of such variant α-amylases each with only a small number of altered amino acids compared to the parent α-amylases. However, the currently claimed genus includes variant α-amylases with any number of alterations of the parent enzyme as long as amylase activity is maintained. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of having α-amylase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 68-72, 86-90, 104-108, and 122-126 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a variant of a parent α-amylase having at

least 80% homology to SEQ ID NO:3 wherein said variant has at least 80% identity to said parent α-amylase, has α-amylase activity and comprises of one or more mutations selected from the group consisting of deletion of residues equivalent to 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3 does not reasonably provide enablement for any variant of a parent α-amylase having at least 80% homology to SEQ ID NO:3 wherein said variant has α-amylase activity and comprises of one or more mutations selected from the group consisting of deletion of residues equivalent to 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 68-72, 86-90, 104-108, and 122-126 are so broad as to encompass any variant of a parent α-amylase having at least 80% homology to SEQ ID NO:3 wherein said variant has α-amylase activity and comprises of one or more mutations selected from the group consisting of deletion of residues equivalent to 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3. Thus, the currently claimed genus includes variant α-amylases with any number of alterations of the parent enzyme as long as amylase activity is maintained. The scope of the claims is not

commensurate with the enablement provided by the disclosure with regard to the extremely large number of variant α-amylases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to only a few representative species of such variant α-amylases each with only a small number of altered amino acids compared to the parent α-amylases.

While recombinant and mutagenesis techniques are known, it is <u>not</u> routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish

with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any because the specification does **not** establish: (A) regions of the protein structure which may be multiply modified without effecting α-amylase activity; (B) a rational and predictable scheme for major modifications to α-amylases having 80% homology to SEQ ID NO:3 at large numbers of residues with an expectation of obtaining the desired biological function; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any variant of a parent α-amylase wherein said variant has α-amylase activity and comprises of one or more mutations selected from the group consisting of deletion of residues equivalent to 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re

Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of α-amylases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

It is noted that amending Claim 68, 86, 104, and 122 to insert "has at least 80% sequence identity to said parent α-amylase," following "wherein said variant" would overcome the rejections under 35 U.S.C. 112, first paragraph above.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 68-71, 73, 75-77, 86-89, 91, 93-95, 104-107, 109, 111-113, 122-125, 127, and 129-131 are rejected under the

judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-23 of U.S. Patent No. 6,297,038. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each recite *Bacillus* alpha amylase variants having a deletion of a pair of residues equivalent to positions 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3. The claims differ in that in the patent the claims also recite additional variants not included in the scope of the instant claims and in that the scope of the parent enzymes in the patented claims and the instant claims differs. It would have been obvious to one of ordinary skill in the art to select any of the specifically defined embodiments of the group of variants recited in the claims of the prior patent which include *Bacillus* alpha amylase

variants having a deletion of a pair of residues equivalent to positions 180 and 181, 179 and 181, 179 and 182, or 180 and 182 of SEQ ID NO:3. Furthermore, it would have been obvious to one of ordinary skill in the art to select any of the enzymes of SEQ ID NOS:1, 2, 3, or 7 as the parent alpha amylase as these are disclosed in the prior patent as the preferred parent enzymes. This specific embodiment of the claims of the prior patent anticipates the claims of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652